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Zeichen/Ref./Réf.	Anmeldung Nr./Application No./Demande n°/Patent Nr./Patent No./Brevet n°
P35145EP-K/NJL	01959277.9-2405/US0123510

Anmelder/Applicant/Demandeur//Patentinhaber/Proprietor/Titulaire
The Johns Hopkins University School of Medicine

COMMUNICATION

The European Patent Office herewith transmits the supplementary partial European search report under Rule 46(1) EPC relating to the above-mentioned European patent application.

Copies of the documents cited in the search report are enclosed.

The applicant's attention is drawn to the following:

The search Division informs the applicant that if the European search report is also to cover inventions other than the invention first mentioned in the claims, a further search fee must be paid for each of these inventions, within ONE MONTH after notification of this communication.

If the application has been filed up to 30 June 1999, the search fee in force before 01 July 1999 (EUR 869,--) or the equivalent applicable on the date of payment is payable.
This applies also to the search fees requested under Rule 46(1) EPC.
See also OJ EPO 06/1999, 405.

Moreover, the Search Division considers that the present European patent application does not comply with the provisions of the European Patent Convention to such an extent that it is not possible to carry out a meaningful search into the state of the art on the basis of some of the claims; reference is made to sheet C, which is attached to the search report.

☐ The abstract was modified by the Search Division and the definitive text is attached to the present communication.

☒ Additional set(s) of copies of the documents cited in the European search report is (are) attached as well.

EUROPÄISCHES PATENTAMT - DEN HAAG - EUROPEAN PATENT OFFICE - LA HAYE - OFFICE EUROPÉEN DES BREVETS

Note to users of the automatic debiting procedure:

Unless the EPO receives prior instructions to the contrary, the search fee(s) will be debited on the last day of the period for payment. For further details see the Arrangements for the automatic debiting procedure, Supplement to OJ EPO 02/1999.

REGISTERED LETTER

European Patent Office

SUPPLEMENTARY PARTIAL EUROPEAN SEARCH REPORT

under Rule 46, paragraph 1 of the European Patent Convention

Application Number EP 01 95 9217

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X	WO 99/40181 A (UNIV JOHNS HOPKINS MED) 12 August 1999 (1999-08-12) * page 13, line 13 - line 25 * * page 27, line 17 - line 22 * * page 46, line 18 - line 27 * * figures 5,7; example 5 *	1-6,10, 11, 17-19, 21-23, 26-28	C12N15/18 C12N15/90 C07K14/475 C07K16/22 G01N33/50
X	WO 98/33887 A (UNIV JOHNS HOPKINS MED) 6 August 1998 (1998-08-06) * page 11, line 26 - page 12, line 10 * * page 26, line 5 - line 10 * * page 44, line 14 - line 25 * * page 35, line 15 - line 19 * * figures 5,15 *	1-6,10, 11, 17-19, 21-23, 26-28	

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TECHNICAL FIELDS SEARCHED (Int.Cl.7)

C12N
C07K
G01N

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

The present partial European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims.

Place of search	Date of completion of the search	Examiner
Munich	25 March 2004	Tudor, M

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

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EPO FORM 1503 03.82 (P04C23)

European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

Application Number
EP 01 95 9217

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	WO 99/42573 A (BIOSTAR INC) 26 August 1999 (1999-08-26) * page 3, line 34 - page 4, line 10 * * page 5, line 12 - line 20 * * page 29, line 5 - line 20 * * claims 1-32; figures 1,16 *	1-6,10, 11, 17-19, 21-23, 26-28	
X	WO 99/02667 A (GEORGES MICHEL ; GROBET LUC (BE); UNIV LIEGE (BE); PONCELET DOMINIQUE) 21 January 1999 (1999-01-21) * page 26, line 8 - line 9 * * page 26, line 24 - line 25 *	1-6,10, 11, 17-19, 21-23, 26-28	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
X	US 5 827 733 A (MCPHERRON ALEXANDRA C ET AL) 27 October 1998 (1998-10-27) * column 5, line 1 - line 21 * * example 3 *	1-6,10, 11, 17-19, 21-23, 26-28	

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EPO FORM 1503 03.82 (P04C10) 3

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	GONZALEZ-CADAVID N F ET AL: "ORGANIZATION OF THE HUMAN MYOSTATIN GENE AND EXPRESSION IN HEALTY MEN AND HIV-INFECTED MEN WITH MUSCLE WASTING" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 95, no. 25, December 1998 (1998-12), pages 14938-14943, XP000918848 ISSN: 0027-8424 * page 14938, right-hand column, paragraph 3 * * page 14939, left-hand column, paragraph 5 *	1-6,10, 11, 17-19, 21-23, 26-28	
A	MCPHERRON ET AL: "Regulation of skeletal muscle mass in mice by a new TGF-beta superfamily member" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 387, 1 May 1997 (1997-05-01), pages 83-90, XP002085797 ISSN: 0028-0836 * page 84, left-hand column, line 25 - line 40 *	1-6,10, 11, 17-19, 21-23, 26-28	TECHNICAL FIELDS SEARCHED (Int.Cl.7)

EPO FORM 1503 03.82 (P04C10) 3

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claim:

Invention 1: Claims 1-6,10,11,17-19,21-28: An N-terminal prodomain fragment of human promyostatin; a polynucleotide encoding said prodomain; a transgenic non-human organism comprising said polynucleotide; an antibody directed against said prodomain; a virtual representation of said fragment; the use of said fragment in a method for identifying functional portions of said fragment.

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2. claim:

Invention 2: Claims 1-6,7,8,17,21,22,24: A C-terminal mature domain fragment of human promyostatin; a polynucleotide encoding said mature domain; a transgenic non-human organism comprising said polynucleotide; an antibody directed against said mature domain.

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3. claim:

Inventions 3-20: Idem as Inventions 1 and 2 but referring to the N-terminal prodomain and C-terminal mature domain fragments of murine, chicken, rat, baboon, bovine, turkey, porcine, ovine and zebrafish promyostatin, respectively.

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4. claim:

Invention 21: Claims 1-7, 9-12, 14-28: fragments of salmon promyostatin alleles 1 and 2: a mutant salmon promyostatin polypeptide comprising a mutation which disrupts the proteolytic cleavage at the proteolytic cleavage site in said promyostatin; polynucleotides encoding said fragments and said mutant; transgenic non-human organisms comprising said polynucleotides; antibodies directed against said fragments; a virtual representation of said polypeptide; a method of identifying functional peptide portions of the prodomain of said myostatins.

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5. claim:

Inventions 22-31: Claims 1-6, 7, 8, 17, 21, 22, 24: a promyostatin prodomain comprising from about amino acid 20 to about amino acid 262 from human, murine, chicken, rat, baboon, bovine, turkey, porcine, ovine and zebrafish, respectively.

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

6. claim:

Inventions 32-41: Claims 15, 16, 20 and 21: the provision of proteolytic cleavage site mutant human, murine, chicken, rat, baboon, bovine, turkey, porcine, ovine and zebrafish promyostatins, respectively.

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7. claim:

Invention 42: Claims 24, 25 and 27: the provision of a virtual representation of a promyostatin polypeptide or a promyostatin prodomain and their use in identifying functional peptide portions of a myostatin prodomain.

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8. claim:

Invention 43: Claims 26-28: A method for identifying functional peptide portions of a myostatin prodomain.

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1). The claims of the present application refer to peptide portions (fragments) of promyostatins, a method for producing a mutant promyostatin by preventing the normal proteolytic cleavage of the pro-protein thereby producing a nonfunctional myostatin molecule, a virtual representation of a promyostatin polypeptide and the use of said representation in identifying functional peptide portions of the myostatin prodomain which specifically interact with a myostatin polypeptide and, a method for in identifying functional peptide portions of the myostatin prodomain which specifically interact with a myostatin polypeptide by testing the interaction of said peptide portion with a myostatin polypeptide.

2). In assessing whether the requirements of unity of invention of an application are met, identification of the technical features that each solution to a technical problem contributes over the prior art (special technical features) must be made. If then a technical relationship between the solutions, involving one or more of the same special technical features, can be recognised, the requirements of unity of invention are said to be met.

3). Peptide portions (fragments) of promyostatins (GDF 8 or GDF II) were well known in the art before the priority date of the present application, see for example, WO 99/42573 describes fragments of myostatins from the mouse, rat, human, baboon, bovine, porcine, ovine, chicken, turkey and zebrafish. Indeed, the biologically active myostatin is a C-terminal fragment proteolytically cleaved from a pro-protein as stated in McPherron et al. (1997), Nature, vol.387, pp. 83-90 on page 84, left column, lines 37-40. WO99/02667 describes on page 26 lines 8-9 and lines 24-25 a method for producing a dominant negative myostatin mutant

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

by mutating the premyostatin proteolytic cleavage site thereby preventing proteolysis. WO99/40181 describes on page 27 lines 7-22 a method for producing a mutant murine, human, rat or chicken promyostatin by preventing the normal proteolytic cleavage of the preprotein thereby producing a nonfunctional myostatin molecule.

In light of the above mentioned prior art the problems and corresponding solutions of the present application can be summarized as follows:

Problem 1: To provide further fragments of promyostatins

Solution 1: Claims 1-6, 10, 11, 17-19, 21-28: an N-terminal prodomain fragment of human promyostatin; a polynucleotide encoding said prodomain; a transgenic non-human organism comprising said polynucleotide; an antibody directed against said prodomain; a virtual representation of said fragment; the use of said fragment in a method for identifying functional portions of said fragment.
Solution 2: Claims 1-6, 12, 13, 17, 21, 22, 24: a C-terminal mature domain fragment of human promyostatin; a polynucleotide encoding said mature domain; a transgenic non-human organism comprising said polynucleotide; an antibody directed against said mature domain.
Solutions 3-20: Idem as Solutions 1 and 2 but referring to the N-terminal prodomain and C-terminal mature domain fragments of murine, chicken, rat, baboon, bovine, turkey, porcine, ovine and zebrafish promyostatin, respectively
Solutions 22-31: Claims 1-6, 7, 8, 17, 21, 22, 24: a promyostatin prodomain comprising from about amino acid 20 to about amino acid 262 from human, murine, chicken, rat, baboon, bovine, turkey, porcine, ovine and zebrafish, respectively

In light of the above mentioned prior art a further problem and corresponding solutions identified in the present can be summarized as follows:

Problem 2: to provide further myostatins
Solution 21: Claims 1-7, 9-12, 14-28: fragments of salmon promyostatin alleles 1 and 2: a mutant salmon promyostatin polypeptide comprising a mutation which disrupts the proteolytic cleavage at the proteolytic cleavage site in said promyostatin; polynucleotides encoding said fragments and said mutant; transgenic non-human organisms comprising said polynucleotides; antibodies directed against said fragments; a virtual representation of said polypeptide; a method of identifying functional peptide portions of the prodomain of said myostatins.

In light of the above mentioned prior art a further problem and corresponding solutions identified in the present can be summarized as follows:

Problem 3: to provide further promyostatin polypeptides comprising a mutation which disrupts proteolytic cleavage at the proteolytic cleavage site

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

Solutions 32-41: Claims 15, 16, 20 and 21: the provision of proteolytic cleavage site mutant human, murine, chicken, rat, baboon, bovine, turkey, porcine, ovine and zebrafish promyostatins, respectively

In light of the above mentioned prior art a further problem and corresponding solutions identified in the present can be summarized as follows:

Problem 4: To provide a virtual representation of a promyostatin polypeptide
Solution 42: Claims 24, 25 and 27: the provision of a virtual representation of a promyostatin polypeptide or a promyostatin prodomain and their use in identifying functional peptide portions of a myostatin prodomain

In light of the above mentioned prior art a further problem and corresponding solutions identified in the present can be summarized as follows:

Problem 5: to provide a method for identifying functional peptide. portions of a myostatin prodomain
Solution 43: claims 26-28: testing a peptide portion of a myostatin prodomain for its ability to interact with myostatin and detecting said interaction

4). As no technical features can be distinguished which, in the light of the prior art, could be regarded as special technical features on which an unifying concept could be based, there is no single inventive concept underlying the plurality of claimed inventions of the present application.

5).Therefore, an objection to lack of unity of invention has to be raised under Article 82 EPC Consequently, a distinction of separate inventions has been made (1-43), based on technical features. The resulting separate inventions, as presently identified, have been grouped according to the order in which they have been claimed. It should be noted that only invention 1 has been completely searched.

European Patent Office

INCOMPLETE SEARCH SHEET C

Application Number
EP 01 95 9217

Claim(s) not searched:
24,25

Reason for the limitation of the search (non-patentable invention(s)):

Claims 24 and 25 refer to the virtual representation of a promyostatin polypeptide or a portion thereof. The subject-matter of said claims is considered to be merely the presentation of information (Article 52(2)(d) EPC) and is, therefore, not considered to be a patentable invention within the meaning of Article 52(1) EPC. Thus, the above mentioned claims will not be searched.

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 01 95 9217

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25-03-2004

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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82